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10/538,201	03/08/2006	Carmen Barske	PN/4-32761A	1795

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EXAMINER	
WEGERT, SANDRA L	
ART UNIT	PAPER NUMBER
1647	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/538,201	BARSKE ET AL.	
	Examiner	Art Unit	
	SANDRA WEGERT	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *4/23/09*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10-24* is/are pending in the application.

4a) Of the above claim(s) *10-16 and 18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17 and 19-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *09 June 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/6/09, 4/23/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments, and/or Claims

Applicants' amendment filed on 27 February 2009 is acknowledged and entered. Claims 1-9 are cancelled. Claims 10-16 and 18 remain withdrawn. Claims 11 and 15-18 are amended. Claims 19-24 are new and read on the elected invention. The Information Disclosure Statements, submitted 6 March 2009 and 23 April 2009, have been entered and considered.

Currently, claims 17 and 19-24 are under consideration.

Withdrawn Objections and/or Rejections

Informalities- URL's

The objection to the specification because it contained browser-executable code as set forth at p. 2 of the previous Office Action (29 September 2008) is *withdrawn* in view of the amendment which removed all hypertext links from the disclosure (27 February 2009).

Claim Rejections - 35 USC § 112, second paragraph, indefiniteness.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> **The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter that the applicant regards as his invention.**

The rejection of claims 2-6 under 35 U.S.C. 112, second paragraph, for being indefinite for reciting or encompassing the phrase "hypervariable regions," is *withdrawn*. Applicants cancelled claims 2-6 (27 February 2009) and newly-added claims do not recite the phrase.

The rejection of claims 4-6 under 35 U.S.C. 112, second paragraph, for reciting the phrase "direct equivalents thereof" when referring to molecules that bind NOGO epitopes, is *withdrawn*. Applicants cancelled claims 4-6 in the response of 27 February 2009.

35 U.S.C. 101, Product of Nature

The following is a quotation of 35 U.S.C. 101:

> **Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.**

The rejection of Claim 1 under 35 U.S.C. § 101, because the claim previously read on a product of nature, is *withdrawn*. Applicants cancelled claim 1 (27 February 2009). Newly added claims recite language indicating that the binding molecules are "isolated" (23 April 2009).

Claim Rejections- 35 USC § 102

The following are quotations of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> **(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.**

The rejection of claim 1 and 17 under 35 U.S.C. 102(b), for being unpatentable over Chen, et al, (2000, Nature, 403: 434-439) is *withdrawn*. Applicants cancelled claim 1 (27 February 2009). Claim 17 and new claims recite the SEQ ID NOs that comprise the antibody, rather than just an antibody that binds the NOGO antigen as found in Chen, et al.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> **(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.**

The rejection of claim 8 under 35 U.S.C. 103(a), for being unpatentable over Chen, et al, (2000, Nature, 403: 434-439) in view of Bendig, et al, (1996), U.S. Patent No. 5,558,864, is *withdrawn*. Applicants cancelled claim 8 (27 February 2009). Remaining claims and newly added claims recite antibody SEQ ID NO's, rather than just the NOGO antigen and the fact that the antibodies are "chimerized" or "humanized."

Maintained/New Objections and/or Rejections

Typographical-

Claims 19, 20 and 21 are objected to for reciting "SEQ ID NO: X" in an improper format (i.e., without a colon). For example, Claim 19 recites "SEQ ID NO. 13." Appropriate correction is required.

Claim Rejections - 35 USC § 112, second paragraph, indefiniteness.

Claims 17 and 19-24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 19-24 recite the phrase "in sequence" to refer to the

fact that the antibodies comprise the SEQ ID NO's in sequential order. The phrase is indefinite in that it cannot be determined if applicants are referring to the order of the sequences or whether they are simply part of a polypeptide sequence. Changing the phrase to "in sequential order" would be remedial. Claim 17 is included in this rejection because it depends from the previously mentioned claims without resolving the indefiniteness issue therein.

Claim Rejections - 35 USC § 112, first paragraph – scope of enablement.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> **The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.**

Claims 17 and 22-24 are rejected under 35 USC 112, first paragraph, because the specification, while being enabling for an antibody that binds NOGO, comprised of SEQ ID NO: 8, 9 and 10 in the heavy chain and SEQ ID NO: 11, 12 and 13 in the light chain, does not enable variants of the CDR sequences that are at least 90% homologous to SEQ ID NO: 8, 9, 10 and SEQ ID NO: 11, 12, and 13, in the heavy and light chains, respectively. This rejection was previously made over claims 2-7 and 9 for reciting CDR sequences that were 50% homologous to SEQ ID NO: 8, 9 and 10 and SEQ ID NO: 11, 12 and 13. However, the specification is not enabling for the full scope of the claimed antibodies compromising the CDR's, wherein the amino acid sequences are at least 90% homologous to the disclosed CDR sequences, with the assurance that claimed proteins that are functionally equivalent to the disclosed CDR sequences can be made without undue experimentation and with the assurance that they would have the desired property of binding NOGO with high affinity and specificity.

Applicants did not provide arguments concerning this rejection, stating only that: "newly added claims are enabled and that no undue experimentation would be required to practice the claimed invention" (Response, 27 February 2009, p. 8). However, as discussed above and in the previous Office Action (29 September 2008), a small change in the secondary structure of an antibody, even of just one residue in the hypervariable regions, produces a large change in tertiary and quaternary structure, which often changes the affinity and specificity of antibody binding in unexpected ways (Macallum, et al, J. Mol. Biol., 1996), 262: 732–745, of record). Thus, it would require undue experimentation to make and test enough examples of antibodies that are 90% similar to the SEQ ID NO's comprising the CDR's, such that the genus is enabled and the new variants bind NOGO with the same affinity and specificity as the claimed antibodies comprising SEQ ID NO: 8, 9, and 10 and 11, 12 and 13.

35 USC § 112, first paragraph – Written Description.

Claims 17 and 22-24 are also rejected under 35 USC 112, first paragraph, because applicants were not in possession of variants of the antibody CDR sequences that are at least 90% homologous to SEQ ID NO: 8, 9, 10 and SEQ ID NO: 11, 12, and 13, respectively. This rejection was previously made over claims 2-7 and 9 for reciting CDR sequences that were 50% homologous to SEQ ID NO: 8, 9 and 10 and SEQ ID NO: 11, 12 and 13.

Applicants discuss the legal standards for Written Description, which the examiner does not dispute (Response, 27 February 2009, pp. 8 and 9). The examiner takes no issue with the legal tests for Written Description described by Applicants (Response, top of page 9). However, Applicants have not described or shown possession of all antibody polypeptides 90%

homologous to the CDR regions comprising SEQ ID NO: 8, 9 and 10 and SEQ ID NO: 11, 12 and 13, *that are functionally equivalent* to the CDR sequences disclosed. Nor have Applicants described a representative number of species that have 90% homology to peptides consisting essentially of SEQ ID NO: 1, such that it is clear that they were in possession of a genus of polypeptides functionally similar to the antibodies comprising SEQ ID NO: 8, 9 and 10 and SEQ ID NO: 11, 12 and 13.

Applicants argue that "Reduction to practice of a single species encompassed within a genus is sufficient to support written description" (Remarks, p. 9, 27 February 2009) and cite Enzo Biochem (323 F.3d at 966, 63 USPQ2d at 1615).

Contrary to what has been implied by the Applicants in citing this case, "Enzo" concerned the Written Description requirements of a deposited *nucleic acid*. In the Appeal it was decided that reference in the patent Specification to a deposit of genetic material may suffice to describe that material; Appellants were *literally* in possession of the nucleic acids in the claimed genus, since they were present in the deposited cells. The case makes no reference to or discussion of the Written Description of materials that have not yet been made or tested. In the instant Application, the Written Description requirement for the 11C7 antibody comprising SEQ ID NO: 8, 9 and 10 and SEQ ID NO: 11, 12 and 13 has been satisfied by disclosure of the 11C7 antibody comprising SEQ ID NO: 8, 9 and 10 and SEQ ID NO: 11, 12 and 13. However, no other antibodies were made to the NOGO antigen, and none other than 11C7 were used in the examples. As far as use of antibody "3C7" in examples 3-7 (as discussed by applicants, 27 February 2009, p. 9), the examiner could not find the example in which antibody 3C7 was

disclosed or tested in the instant specification.

Applicants also argue that "procedures for making variants of the reference Nogo_A623-640 binding protein which have at least 90% identity to its recited amino acid sequence are conventional in the art" (Response, p. 10). However, applicants must be in *possession* of the claimed variants in order to have adequate Written Description of the claimed subject matter. The fact that current molecular biology techniques allow one to produce antibodies that vary by 10% from the reference sequence, does not mean that there was a reduction to practice such that the variant antibodies were reliably produced and tested for the same activity as the 11C7 antibody disclosed in the instant Specification. Producing an antibody with "changes in only a few amino acids at most" (Response, p. 11), may produce antibodies with unexpected characteristics (as discussed above in the Enablement rejection), or that do not bind the NOGO antigen with the same affinity and specificity as the reference antibody. As discussed in the previous Office Action (29 September 2008), adequate written description requires more than a mere statement that the claimed subject matter is part of the invention, and reference to a potential method of isolating it. The claimed compound *itself* is required (Federal Register, 2001, Vol. 66, No. 4, pages 1099-1111, esp. page 1104, 3rd column).

Conclusion

No claims are allowed.

Note: An attempt was made to negotiate an allowance with applicants' representative on 28 May 2009. However, an agreement could not be reached on the proposed claim amendments.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Advisory information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sandra Wegert whose telephone number is (571) 272-0895. The examiner can normally be reached Monday - Friday from 9:00 AM to 5:00 PM (Eastern Time). If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Manjunath Rao, can be reached at (571) 272-0939.

The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (in USA or CANADA) or 571-272-1000.

SLW
6 June 2009

/Bridget E Bunner/
Primary Examiner, Art Unit 1647